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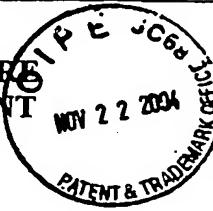
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INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

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Complete if Known

Application Number	10/764,833
Filing Date	January 27, 2004
First Named Inventor	AYALON-SOFFER Michal et al
Group Art Unit	1631
Examiner Name	P. WAVEY

Sheet	1	Of	3	Attorney Docket Number
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS				
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.		T ²
PW		Naka et al, "The paradigm of IL-6: from basic science to medicine" Arthritis Res. 2002;4 Suppl 3:S233-42. Epub 2002 May 09. Review		
PW		Furge et al, "Met receptor tyrosine kinase: enhanced signaling through adapter proteins" Oncogene. 2000 Nov 20;19(49):5582-9.		
PW		Deonarain et al, "Interferon-alpha/beta-receptor interactions: a complex story unfolding", Curr Pharm Des. 2002;8(24):2131-7.		
PW		Blazar et al, "Ligation of 4-1BB (CDw137) regulates graft-versus-host disease, graft-versus-leukemia, and graft rejection in allogeneic bone marrow transplant recipients", J Immunol. 2001 Mar 1;166(5):3174-83.		
PW		Fry et al, "Interleukin-7: from bench to clinic", Blood. 2002 Jun 1;99(11):3892-904		
PW		Attasano et al, "Signal transduction by the TGF-beta superfamily", Science. 2002 May 31;296(5573):1646-7.		
PW		Kerr et al, "Small molecule alpha(v) integrin antagonists: novel anticancer agents", Expert Opin Investig Drugs. 2000 Jun;9(6):1271-9.		
PW		To et al, "The roles of hepatocyte growth factor/scatter factor and met receptor in human cancers (Review)", Oncol Rep. 1998 Sep-Oct;5(5):1013-24		
PW		Simpson et al, "Interleukin-6: structure-function relationships", Protein Sci. 1997 May;6(5):929-55.		
PW		Cosenza et al, "Comparative model building of interleukin-7 using interleukin-4 as a template: a structural hypothesis that displays atypical surface chemistry in helix D important for receptor activation", Protein Sci. 2000 May;9(5):916-26.		
PW		Comoglio et al, "Invasive growth: from development to metastasis", J Clin Invest. 2002 Apr;109(7):857		
PW		Brierley et al, "IFN-alpha/beta receptor interactions to biologic outcomes: understanding the circuitry", J Interferon Cytokine Res. 2002 Aug;22(8):835-45.		
PW		Aggarwal, BB, "Signalling pathways of the TNF superfamily: a double-edged sword", Nat Rev Immunol. 2003 Sep;3(9):745-56		
PW		Tucker, GC, "αv Integrin inhibitors and cancer therapy", Curr Opin Invest Drugs, 4(6):722-731,2003		
PW		Nelms et al, "The IL-4 receptor: signaling mechanisms and biologic functions", Annu Rev Immunol. 1999;17:701-38		
PW		Moor et al, "Interleukin-10 and the interleukin-10 receptor", Annu Rev Immunol. 2001;19:683-765.		
PW		Pan et al, "IL-4 receptor mutations", Curr Opin Immunol. 1999 Dec;11(6):615-20.		
PW		Seo et al, "Blocking 4-1BB/4-1BB ligand interactions prevents herpetic stromal keratitis", J Immunol. 2003 Jul 15;171(2):576-83.		
PW		Vinay et al, "Role of 4-1BB in immune responses", Semin Immunol. 1998 Dec;10(6):481-9.		

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Examiner Name	P. WINNIET

Sheet	2	Of	3	Attorney Docket Number	27256
PW		Zhang et al "HGF/SF-met signaling in the control of branching morphogenesis and invasion", J Cell Biochem. 2003 Feb 1;88(2):408-17.			
PW		Walter, MR, "Strucure of interleukin-10/interleukin-10R1 complex: a paradigm for class 2 cytokine activation", Immunol Res. 2002;26(1-3):303-8.			
PW		Gessner et al, " Biologic functions and signaling of the interleukin-4 receptor complexes", Immunobiology. 2000 Jan;201(3-4):285-307			
PW		Croft M, "Costimulation of T cells by OX40, 4-1BB, and CD27", Cytokine Growth Factor Rev. 2003 Jun-Aug;14(3-4):265-73			
PW		Hirano T, "Interleukin 6 and its receptor: ten years later", Int Rev Immunol. 1998;16(3-4):249-84.			
PW		Asadullah et al, " Interleukin-10 therapy--review of a new approach", Pharmacol Rev. 2003 Jun;55(2):241-69.			
PW		Meuller et al, " Structure, binding, and antagonists in the IL-4/IL-13 receptor system", Biochim Biophys Acta. 2002 Nov 11;1592(3):237-50.			
PW		VanderSpek et al, " Structure function analysis of interleukin 7: requirement for an aromatic ring at position 143 of helix D", Cytokine. 2002 Mar 7;17(5):227-33.			
PW		Kotenko SV, "The family of IL-10-related cytokines and their receptors: related, but to what extent?", Cytokine Growth Factor Rev. 2002 Jun;13(3):223-40			
PW		Wrana JL, "TGF-beta receptors and signalling mechanisms", Miner Electrolyte Metab. 1998;24(2-3):120-30			
PW		Kwon et al, " 4-1BB: still in the midst of darkness", Mol Cells. 2000 Apr 30;10(2):119-26.			
PW		Miyazono K, "TGF-beta receptors and signal transduction", Int J Hematol. 1997 Feb;65(2):97-104.			
PW		Brattain et al, " The type II transforming growth factor-beta receptor as a tumor-suppressor gene", Curr Opin Oncol. 1996 Jan;8(1):49-53.			
PW		Bihl et al, " Identification of a novel IL-6 isoform binding to the endogenous IL-6 receptor", Am J Respir Cell Mol Biol. 2002 Jul;27(1):48-56.			
PW		Maulik et al, " Role of the hepatocyte growth factor receptor, c-Met, in oncogenesis and potential for therapeutic inhibition", Cytokine Growth Factor Rev. 2002 Feb;13(1):41-59.			
PW		Gorgun et al, " Altered biological activity associated with C-terminal modifications of IL-7", Cytokine. 2002 Oct 7;20(1):17-22.			
PW		Mark et al, " Expression and characterization of hepatocyte growth factor receptor-IgG fusion proteins. Effects of mutations in the potential proteolytic cleavage site on processing and ligand binding", J Biol Chem. 1992 Dec 25;267(36):26166-71.			
PW		Mould et al, " Molecular basis of ligand recognition by integrin alpha Sbeta 1. I. Specificity of ligand binding is determined by amino acid sequences in the second and third NH2-terminal repeats of the alpha subunit", J Biol Chem. 2000 Jul 7;275(27):20324-36.			
PW		Moustakas et al, " Smad regulation in TGF-beta signal transduction", J Cell Sci. 2001 Dec;114(Pt 24):4359-69			

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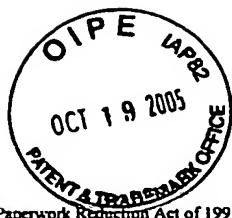
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U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ³ (if known)			
PW	1	US-2004/0101876	05-27-2004	Mintz et al.	
PW	2	US-2004/0142325	07-22-2004	Mintz et al.	
PW	3	US-2004/0248157	09-9-2004	Ayalon-Soffer et al.	

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PW	10	Tullo et al. "Reorganization and Merging of the EMBL and GenBank Keyword Indexes in A Tree Structure for More Efficient Retrieval of Nucleic Acid Sequences", Protein Sequences and Data Analysis, 3: 327-334, 1990.	
PW	11	Shoshan et al. "Designing Oligo Libraries Taking Alternative Splicing Into Account", Proc. SPIE., 4266: 86-95.	
PW	12	Michel et al. "Identification of A Novel IL-6 Isoform Binding to Endogenous IL-6 Receptor", Annual Journal Respir. Cell Molecular Biology, 27: 48-56, 2002.	
PW	13	Croft "Costimulatory Members of the TNFR Family: Keys to Effective T-Cell Immunity?" Nature Reviews, 3: 609-, 2003.	
PW	14	Aigner et al. "Expression of A Truncated 100 kDa HER2 Splice Variants Acts as An Endogenous Inhibitor of Tumour Cell Proliferation", Oncogene, 20(17): 2101-2111, 2001.	
PW	15	Gebhardt et al. "Differential Expression of Alternatively Spliced C-ErB-2 mRNA in Primary Tumors, Lymph Node Metastases, and Bone Marrow Micrometastases From Breast Cancer Patients", Biochemical and Biophysical Research Communications, 247(2): 319-323, 1998.	
PW	16	Kwong et al. "A Novel Splice Variant of HER2 With Increased Transformation Activity", Molecular Carcinogenesis, 23(2): 62-68, 1988.	
PW	17	Azios et al. "Expression of Herstatin, An Autoinhibitor of HER-2/Neu, Inhibits Transactivation of HER-3 by HER-2 and Blocks EGF Activation of the EGF Receptor", Oncogene, 20(37): 5199-5232, 2001.	
PW	18	Strausberg et al. "Homo Sapiens Ubiquitin-Conjugating Enzyme E2C, mRNA (cDNA Clone IMAGE: 5574059), Partial Cds", Database EMBL 'Online! Database Accession No. BC032677, 2202. See: "Generation and Initial Analysis of More Than 15,000 Full-Length Human and Mouse cDNA Sequences", Proc. Natl. Acad. Sci. USA, 99(26): 16899-16903, 2002.	
PW	19	??? "AGENCOURT_6578352 NIH_MGC_41 Homo Sapiens cDNA Clone IMAGE: 5467535 5', mRNA Sequence", Database EMBL 'Online!, Database Accession No. BM556795, 2002.	
PW	20	??? "AGENCOURT_7952308 NIH_MGC_72 Homo Sapiens cDNA Clone IMAGE: 6149711 5', mRNA Sequence", Database EMBL 'Online!, Database Accession No. BU171488, 2002.	
PW	21	Townsley et al. "Dominant-Negative Cyclin-Selective Ubiquitin Carrier Protein E2-C/UBCH10 Blocks Cells in Metaphase", Proc. Natl. Acad. Sci. USA, 94(6): 2362-2367, 1997.	
PW	22	Schlegel et al. "Human Cervical Cancer Cell Marker Protein SEQ ID NO: 228", Database Geneseq 'Online!, Database Accession No. ABR92159, 2003. & WO 02/101075, 2002.	
PW	23	Okamoto et al. "UbcH10 Is the Cancer-Related E2 Ubiquitin-Conjugating Enzyme", Cancer Research, 63(14): 4167-4173, 2003.	
PW	24	??? "OTTHUMP00000031654 (Fragment)", Database EMBL, Database Accession No. Q9BQP0, 2001. Abstract.	
PW	25	Reeck et al. "'Homology' in Proteins and Nucleic Acids: A Terminology Muddle and A Way Out of It", Cell, 50: 667, 1987.	
PW	26	??? "AGENCOURT_785234 NIH_MGC_67 Homo Sapiens cDNA Clone IMAGE: 6140098 5', mRNA Sequence", Database EMBL 'Online!, Database Accession No. BU169315, 2002.	

PW	27	Krawczak et al. "The Mutational Spectrum of Single Base-Pair Substitutions in mRNA Splice Junctions of Human Genes: Causes and Consequences", Human Genetics, 90: 41-54, 1992.	
PW	28	Boguski et al. "ESTablishing A Human Transcript Map", Nature Genetics, 10: 369-371, 1995.	
PW	29	Schena et al. "Quantitative Monitoring of Gene Expression Patterns With A Complementary DNA Microarray", Science, 270: 467-470, 1995.	
PW	30	Velculescu et al. "Serial Analysis of Gene Expression", Science, 270: 484-487, 1995.	
PW	31	Hillier et al. "Generation and Analysis of 280,000 Human Expressed Sequence Tags", Genome Research, P. 807-828.	
PW	32	Dwight et al. "Saccharomyces Genome Database (SGD) Provides Secondary Gene Annotation Using the Gene Ontology (GO)", Nucleic Acids Research, 30(1): 69-72, 2002.	
PW	33	Matloubian et al. "A Transmembrane CXC Chemokine Is A Ligand for HIV-Coreceptor Bonzo", Nature Immunology, 1(4): 298-304, 2000.	
PW	34	David et al. "Unusual Alternative Splicing Within the Human Kallikrein Genes KLK2 and KLK3 Gives Rise to Novel Prostate-Specific Proteins", The Journal of Biological Chemistry, 277(20): 18084-18090; 2002.	
PW	35	Camargo et al. "The Contribution of 700,000 ORF Sequence Tags to the Definition of the Human Transcriptome", PNAS, 98(21): 12103-12108, 2001.	
PW	36	Caron et al. "The Human Transcriptome Map: Clustering of Highly Expressed Genes in Chromosomal Domains", Science, 291: 1289-1292, 2001.	
PW	37	Audic et al. "The Significance of Digital Gene Expression Profiles", Genome Research, 7: 986-995, 1997.	
PW	38	Huminiecki et al. "In Silico Cloning of Novel Endothelial-Specific Genes", Genome Research, 10: 1796-1806, 2000.	
PW	39	Kawamoto et al. "BodyMap: A Collection of 3' ESTs for Analysis of Human Gene Expression Information", Genome Research, 10: 1817-1827, 2000.	
PW	40	Liu et al. "A Mechanism for Exon Skipping Caused by Nonsense or Missense Mutations in BRCA1 and Other Genes", Nature Genetics, 27: 55-58, 2001.	
PW	41	Brett et al. "EST Comparison Indicates 38% of Human mRNAs Contain Possible Alternative Splice Forms", FEBS Letters, 474: 83-86, 2000.	
PW	42	Croft et al. "ISIS, the Intron Information System, Reveals the High Frequency of Alternative Splicing in the Human Genome", Nature Genetics, 24: 340-341, 2000.	
PW	43	Burset et al. "Analysis of Canonical and Non-Canonical Splice Sites in Mammalian Genomes", Nucleic Acids Research, 28(21): 4364-4375, 2000.	
PW	44	Boguski "Biosequence Exegesis", Science, 286: 453-455, 1999.	
PW	45	Doherty et al. "The HER-2/Neu Receptor Tyrosine Kinase Gene Encodes A Secreted Autoinhibitor", Medical Sciences, 96(19): 10869-10874, 1999.	
PW	46	Nahta et al. "Growth Factor Receptors in Breast Cancer: Potential for Therapeutic Intervention", The Oncologist, 8(1): 5-17, 2003.	
PW	47	Younes et al. "Labelled Oligonucleotides as Radiopharmaceuticals: Pitfalls, Problems and Perspectives", Current Pharmaceutical Design, 8: 1451-1466, 2002.	
PW	48	Sazani et al. "Modulation of Alternative Splicing by Antisense Oligonucleotides", Progress in Molecular and Subcellular Biology, 31: 217-239, 2003.	

Signature	/Pablo Whaley/ (08/07/2006)	Considered
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